CLAIMS

1. A conjugate comprising

a) a trifunctional cross-linking moiety, to which is coupled

b) an affinity ligand via a linker 1 containing hydrogen bonding atoms and chosen from the group consisting of ethers, thioethers, carboxylates, sulfonates, amines, and ammonium groups,

c) a cytotoxic agent, optionally via a linker 2, and

d) an anti Erb antibody or variants thereof having the ability to bind to Erb antigens with an affinity-binding constant of at least $5x10^6M^{-1}$, wherein in average 2-4 molecules of the part a)-c) above are linked to the anti Erb antibody,

wherein the affinity ligand is biotin, or a biotin derivative having essentially the same binding function to avidin or streptavidin as biotin, wherein stability towards enzymatic cleavage of the biotinamide bond has been introduced in linker 1.

2. The conjugate according to claim 1, wherein the anti Erb antibody or variants thereof are directed to Erb 1, Erb 2, Erb 3, and/or Erb 4 antigens expressed on mammalian tumour surfaces.

3. The conjugate according to claim 1 or 2, wherein the anti Erb antibody variants are any modifications, fragments or derivatives of the anti Erb antibody having the same or an essentially similar affinity-binding constant of at least $5x10^6\ M^{-1}$ when binding to the Erb antigen, said fragments comprising Fab, Fab', F(ab')2, F(ab'') and Fv fragments; diabodies; single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

4. The conjugate according to any one of the preceding claims, wherein the anti Erb antibody is coupled to the trifunctional cross-linking moiety via a linker 3, and wherein the bond formed between linker 3 and the anti Erb antibody is either covalent or non-covalent with a binding affinity constant of at least $5x10^8$ M^{-1}.

5. The conjugate according to any one of the preceding claims, wherein the cytotoxic agent is a radionuclide, chemotherapeutical agents, a synthetic or naturally occurring toxin, immunosuppressive or immunostimulating agents, radiosensitizers, enhancers for X-ray or MRI or ultrasound, non-radioactive elements, which can be converted to radioactive elements by means of external irradiation after the anti Erb antibody carrying said element has been accumulated to specific cells or tissues, or photoactive compounds or compounds used in photo imaging or photodynamic therapy, or any other molecule having the same or a similar effect, directly or indirectly, on cancer cells or cancer tissues.

6. The conjugate according to any one of the preceding claims, wherein the cytotoxic agent is a radionuclide, a chemotherapeutical agent, or a toxin.

7. The conjugate according to claim 6, wherein when the cytotoxic agent is a radionuclide it is bound to the trifunctional cross-linking moiety via a cytotoxic agent binding moiety.

8. The conjugate according to claim 7, wherein the cytotoxic agent binding moiety form aryl halides and vinyl halides for radionuclides of halogens, and comprises N_2S_2 and N_3S chelates for Tc and Re radionuclides, amino-carboxy derivatives, preferably EDTA, triethylenetetraaminehexaacetic acid, and DTPA or derivatives thereof, wherein the DTPA derivatives are Me-DTPA, CITC-DTPA, and cyclohexyl-DTPA, and cyclic amines, preferably NOTA, DOTA and TETA, and derivatives thereof, for In, Y, Pb, Bi, Cu, Sm and Lu radionuclides, or any other radionuclide capable of forming a complex with said chelates.

9. The conjugate according to claims 7 and 8, wherein the cytotoxic agent binding moiety comprises DOTA and the cytotoxic agent is ^{90}Y for therapeutic application or ^{111}In for diagnostic application.

10. The conjugate according to claims 6 and 7, wherein the cytotoxic agent binding moiety comprises DOTA and the cytotoxic agent is ^{177}Lu for both diagnostic and therapeutic application.

11. The conjugate according to claim 10, wherein the radionuclide is a beta radiation emitter, preferably scandium-46, scandium-47, scandium-48, copper-67, gallium-72, gallium-73, yttrium-90, ruthenium-97, palladium-100, rhodium-101, palladium-109, samarium-153, lutetium-177, rhenium-186, rhenium-188, rhenium-189, gold-198, and radium-212; a gamma emitter, preferably ioidine-131, lutetium-177 and indium-m 114; or alpha radiation emitting materials, preferably bismuth-212, bismuth-213 and astatine-211; as well as positron emitters, preferably gallium-68 and zirconium-89, wherein the chemotherapeutical agent is Adriamycin, Doxorubicin, 5-Fluorouracil, Cytosine arabinoside ("Ara-C"), Cyclophosphamide, Thioptepa, Busulfan, Cytoxin, Taxol, Methotrexate, Cisplatin, Melphalan, Vinblastine, Bleomycin, Etoposide, Ifosfamide, Mitomycin C, Mitoxantrone, Vincristine, Vinorelbine, Carboplatin, Tenisposide, Duanomysin, Carminomycin, Aminopterin, Dactinomycin, Mitomycins, Esperamicins, Maytansinoid, Melphalan and other related nitrogen mustards; and wherein the toxin is an active toxin of bacterial, fungal, plant or animal origin, or fragments thereof.

12. The conjugate according to any one of the preceding claims, wherein the affinity ligand is a moiety which binds specifically to avidin, streptavidin or any other derivatives, mutants or fragments of avidin or streptavidin having essentially the same binding function to this affinity ligand.

13. The conjugate according to any one of the

preceding claims, wherein the biotin derivative is chosen from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, destibiotin, diaminobiotin, biotin sulfoxide, and biotin sulfone, or derivatives thereof having essentially the same binding function, preferably with an affinity-binding constant of at least $10^9\ M^{-1}$.

14. The conjugate according to any one of the preceding claims, wherein the trifunctional cross-linking moiety is chosen from the group consisting of triaminobenzene, tricarboxybenzene, dicarboxyanyline and diaminobenzoic acid.

15. The conjugate according to any one of the preceding claims, wherein linker 1 serves as an attaching moiety and a spacer between the trifunctional cross-linking moiety and the affinity ligand, preferably a biotin moiety, such that binding with avidin or streptavidin, or any other biotin binding species, is not diminished by steric hindrance.

16. The conjugate according to any one of the preceding claims, wherein the stability towards enzymatic cleavage, preferably against cleavage by biotinidase, of the biotin amide bond to release biotin has been provided by introducing a methyl group on the biotinamide amine or an alpha carboxylate, a hydroxymethyl, or a methyl group or ethyl group on an atom adjacent, preferably less than three carbon atoms apart, to the biotinamide amine.

17. The conjugate according to claim 16, wherein in the case of a hydroxymethyl group the stability has been attained by the introduction of a serinyl group, and wherein in the case of a carboxyl group the stability has been attained by the introduction of an α or β aspartyl group.

18. The conjugate according to any one of the preceding claims, wherein linker 2 provides a spacer length of 1-25 atoms, preferably a length of 6-18 atoms.

19. The conjugate according to claim 18, wherein

linker 2 contains hydrogen bonding atoms, preferably ethers or thioethers, or ionisable groups, to aid in water solubilisation.

20. The conjugate according to any one of claims 1-17, wherein linker 2 is excluded.

21. The conjugate according to any one of the preceding claims, wherein linker 3 provides a spacer of a length of 1-25 atoms, preferably a length of 6-18 atoms, or groups of atoms.

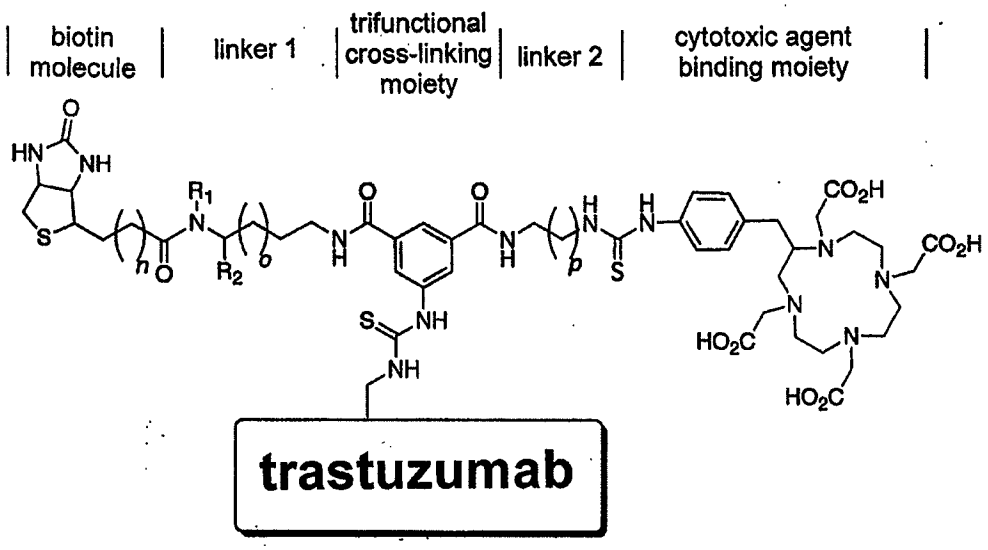
22. The conjugate according to claim 21, wherein linker 3 contains hydrogen bonding atoms such as ethers or thioethers, or ionisable groups, preferably carboxylates, sulfonates, or ammonium groups, to aid in water solubilisation.

23. The conjugate according to any one of claims 1-3 and 5-20, wherein linker 3 is excluded.

24. The conjugate according to any one of the preceding claims, wherein more than one affinity ligand, preferably two, and/or more than one cytotoxic agent, preferably two, also are bound.

25. The conjugate according to any one of the preceding claims, wherein in average 2.5-3.5 molecules of the part a)-c) of the conjugate are linked to each anti Erb antibody.

26. The conjugate according to any one of the preceding claims, wherein it is



wherein n is 2-4 , o is 1-6, p is 1-6, R_1 is H, and R_2 is -COOH, and wherein n preferably is 3, o preferably is 3, and p preferably is 3, bound to a cytotoxic agent via the cytotoxic agent binding moiety.

27. The conjugate according to any one of claims 1-25, wherein it is ^{177}Lu-1033-trastuzumab, i.e. ^{177}Lu-3-(13'-thioureabenzyl-DOTA)trioxadiamine-1-(13"-biotin-Asp-OH)trioxadiamine-5-isothiocyanato-aminoisophtalate-trastuzumab; ^{90}Y-1033-trastuzumab; ^{111}In-1033-trastuzumab; 1033-trastuzumab, wherein thioureabenzyl-DOTA has been replaced with maytansinoid; and 1033-trastuzumab, wherein thioureabenzyl-DOTA has been replaced with doxorubicin, wherein it preferably is trastuzumab with in average 2.2 MitraTag™-1033 molecules bound thereto.

28. A medical composition, wherein it comprises the conjugate according to any one of claims 1-27 together with a pharmaceutically acceptable excipient.

29. The medical composition according to claim 28, wherein the excipient is a solution intended for parenteral administration, preferably intravenous administration.

30. A kit for extracorporeal removal of or at least reduction of the concentration of a non-tissue bound medical composition as defined in any one of claims 28

and 29, comprising a conjugate according to any one of claims 1-26, in the plasma or whole blood of a mammalian host, wherein said medical composition has previously been introduced in the body of said mammalian host and kept therein a certain time in order to be concentrated to the specific tissues or cells by being attached thereto, said kit comprising

a) said medical composition, and

b) an extracorporeal device comprising an immobilized receptor onto which the affinity ligand of the conjugate adheres.

31. The kit according to claim 30, wherein it comprises antibodies and antigens/haptens or protein and cofactors as affinity ligand/immobilized receptor combinations, preferably biotin or biotin derivatives as affinity ligands and avidin or streptavidin as the immobilized receptor.

32. The kit according to claim 30, wherein the affinity ligand is absent in the conjugate of the medical composition, and the immobilized receptor is molecularily imprinted polymers interacting with the conjugate.

33. A method for the treatment of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to any one of claims 28 and 29 is administered to the mammal in need thereof.

34. The method according to claim 33, wherein said cancer is breast or ovarian cancer.

35. The method according to claims 33 and 34, wherein said cancer is breast cancer, preferably of Erb 2 type.

36. The method accoding to any one of claims 33-35, wherein a medical composition according to claims 28 and 29 containing ^{90}Y as the cytotoxic agent in a dose of 10-20 MBq/kg body weight, preferably 11-15 MBq/kg body weight, is administered to the mammalian host.

37. The method according to any one of claims 33-35, wherein a medical composition according to claims 28 and 29 containing ^{90}Y as the cytotoxic agent in a dose of more than 20 MBq/kg body weight is administered to the mammalian host together with means to reconstitute the bone marrow or by reduction of the radiation effect on the bone marrow.

38. A method for diagnosing cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to any one of claims 28 and 29 is administered to the mammalian host.

39. The method according to claim 38, wherein said cancer is breast or ovarian cancer.

40. The method according to claims 38 and 39, wherein said cancer is breast cancer, preferably of Erb 2 type.

41. The method according to any one of claims 38-40, wherein ^{111}In in a dose of 50-200 MBq/m^2 body surface, preferably 100-150 MBq/m^2 body surface, is administered to the mammalian host.

42. A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition acording to claims 28 and 29 containing ^{111}In in a dose of 50-200 MBq/m^2 body surface, preferably 100-150 MBq/m^2 body surface, and a medical composition according to claims 28 and 29 containing ^{90}Y as a cytotoxic agent in a dose of 10-20 MBq/kg body weight, preferably 11-15 MBq/kg body weight, are administered to the mammalian host.

43. A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to claims 28 and 29 containing ^{111}In in a dose of 100-150 MBq/m^2 body surface, and a medical composition according to claims 28 and 29 containing ^{90}Y as the cytotoxic agent in a dose of more than >20 MBq/kg body

weight, are administered to the mammalian host, either in sequence in said order by a time interval of 6-8 days or simultaneously.

44. A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to claims 28 and 29 containing ^{177}Lu as the cytotoxic agent in a single dose of 555-2220 MBq/m^2 body surface, preferably 1000-2000 MBq/m^2 body surface, is administered to the mammalian host.

45. A method for treatment and diagnosing of cancer expressing Erb gene products on the surface of its tumour cells in a mammalian host, wherein a medical composition according to claims 28 and 29 containing ^{177}Lu as the cytotoxic agent in a single dose of more than 2220 MBq/m^2 body surface is administered to the mammalian host together with means to reconstitute the bone marrow or by reduction of the radiation effect on the bone marrow.